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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,261	10/29/2003	James M. Wilson	K1774DIV2	7899

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/696,261	WILSON ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-12* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Final Rejection

Claims 6-13 are pending.

Applicant's traversal, the amendment to the specification, the amendment to claims 6, 7, and 9 and the addition of claims 11-13 in paper filed on 6/5/06 is acknowledged and considered by the examiner.

Claim Objections

Claim 12 is objected to because of the following informalities: the phrase "with one or more a Phe.." in line 2 is grammatically improper. Suggest amending the phrase to recite: --with one or more substitutions at an amino acid selected from the group consisting (comprising) --. Appropriate correction is required.

Claim 13 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New matter rejection:

New claims 11 and 12 are not supported by the instant specification. There appears to be no written description for a method of delivering a heterologous nucleic acid to at least one muscle cell in a mammalian subject comprising providing at least one rAAV comprising an AAV-6 capsid and comprising a heterologous nucleic acid molecule comprising a nucleic acid sequence encoding, wherein **the nucleic acid molecule comprises two AAV2 inverted terminal repeats (ITRs)** in the application as filed. In addition, there appears to be no written description for the rAAV comprising an AAV6 capsid having an amino acid sequence of SEQ ID NO: 13 with an Asp at position 419 of SEQ ID NO: 13 or using it in the claimed method. See MPEP § 2163.06. Applicants cite page 23, line 10 for support for claim 11 and page 24, lines 6-10 for support for claim 12. Page 23, line 10 does not disclose using a nucleic acid molecule comprising two AAV2 ITRs in the claimed method. Page 23, line 10 only recites, "so far there is no report on AAV-6 with two AAV-2 ITRS." Page 24, lines 6-10 does not disclose an Asp at position 419 of SEQ ID NO: 13 and using a rAAV with the AAV-6 capsid having an amino acid sequence of SEQ ID NO: 13 with one or more substitutions at position 129, 419, 531, 584, 598, and 642 of SEQ ID NO: 13 in the claimed method. In addition, SEQ ID NO: 13 is directed to AAV-1 VP1 not an AAV-6 capsid protein. Therefore, there is nothing in the specification that supports the in vivo methods as set forth in the instant claims.

"It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The phrase "an amino acid sequence of SEQ ID NO: 13 with one or more" in instant claim 12 reads on any amino acid sequence having an amino acid sequence of SEQ ID NO: 13 having a Phe at 129, Asp at 419, Lys at 531, Leu at 584, Val at 598, His at 642 of the sequence.

Claims 6-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell (W) taken with Flotte et al. (US 6,461,606). Russell teaches a method of delivering a heterologous nucleic acid to a muscle cell comprising administering to a muscle cell a recombinant adeno-associated virus 6 (rAAV-6) comprising a nucleic acid encoding a protein operably linked to a promoter (columns 3, 24-27, and 72). One of ordinary skill in the art would understand that muscles have veins. Thus, delivering AAV6 to a muscle cell in vivo would read on delivering the AAV6 to veins in the muscle. Russell further teaches the availability of AAV viral vectors based on AAV3A, AAV3B or AAV6 provides an opportunity to use such vectors in patients that previously have generated a viral neutralizing immune response against AAV2 (column 10). Russell teaches the limitation of instant claim 16 (AAV VP 1 protein from four different AAV sequences, See Figure 2). However, Russell does not specifically teach using alpha1-antitrypsin as the protein in the method or delivering the rAAV to skeletal muscle.

However, at the time the invention was made, Flotte teaches the delivering rAAV comprising alpha1-antitrypsin (AAT) to skeletal muscle cells was well known to one of ordinary skill in the art (abstract and columns 1 and 81).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Russell taken with Flotte et al., namely to use

alpha1-antitrypsin in the method taught by Russell. One of ordinary skill in the art would have been motivated to combine the teaching and use AAV-6 comprising a nucleic acid encoding alpha1-antitrypsin as the protein in the method taught by Russell because the availability of an AAV viral vector based on AAV6 provides an opportunity to use such a vector in patients that previously have generated a viral neutralizing immune response against AAV2. In addition, Flotte teaches that AAV can be used by one of ordinary skill in the art to sufficiently deliver and express AAT in muscle cells in vivo.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Russell taken with Flotte, namely to deliver the rAAV-6 to skeletal muscle. One of ordinary skill in the art would have been motivated to combine the teaching to deliver the rAAV-6 to skeletal muscle cells to achieve sustained expression of AAT in vivo.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 6/5/06 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that Russell requires that AAV genomic sequence other than a polypeptide of the AAV6 capsid protein be present in the construct and there is not

explicit teaching of a viral vector containing a full AAV6 capsid, the argument is not found persuasive because Russell teaches delivering an AAV6 viral vector to a cell, wherein the AAV6 comprises an AAV6 capsid protein (see column 72, claim 26).

In addition, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., full AAV6 capsid) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Response to Arguments

Applicant's arguments, see page 8, filed 6/5/06, with respect to 102(e) by Russell have been fully considered and are persuasive. The rejection of claims 1, 2, 4, 7, and 9-10 has been withdrawn because of the cancellation of claims 1, 2, and 4 and the amendment to claims 7 and 9.

Applicant's arguments, see page 8, filed 6/5/06, with respect to 102(e) by High have been fully considered and are persuasive. The rejection of claims 1, 2, 4, and 6-10 has been withdrawn because of the cancellation of claims 1, 2, and 4 and the amendment to claims 6, 7 and 9.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman

BRIAN WHITEMAN
PATENT EXAMINER